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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/741,669	12/19/2000	R. Allyn Forsyth	ELITRA.009A	7061

20995 7590 01/08/2004

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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/741,669	FORSYTH ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-56,128 and 132-134* is/are pending in the application.

4a) Of the above claim(s) *128 and 132* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-56,133 and 134* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 December 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3/2003* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *12/03*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action and applicant's declaration under 37 C.F.R § 1.132 filed on August 11, 2003 have been entered. After carefully consider applicant's request for reconsideration of the finality of the rejection of the last Office action, the finality of that action has been withdrawn since the examiner did not indicate that claim 132 is a non-elected invention in last office action. However, since amended claims 128 and 132 are directed to a method for manufacturing an antibiotic while claim 45, which claims 128 and 132 are dependent on, is directed to a method for identifying a compound, claims 128 and 132 are not considered to be independent or distinct from the invention originally claimed wherein original filed claim 128 comprises a screening step using the method of claim 45. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 128 and 132 have been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Since claims 1-44, 57-127, and 129-131 have been canceled and new claims 133 and 134 have been added, the claims pending in this application are claims 45-56, 128, and 132-134 with claims 128 and 132 withdrawn from consideration as the result of the restriction requirement. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the amendment filed on August 11, 2003. Claims 45-56, 133, and 134 will be examined.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Written Description

Claims 133 and 134 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the interim guidelines on written description published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp.71427-71440.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

The specification (page 50 and sequencing listing) provides adequate written descriptions for SEQ ID NOs: 220 and 413, which are a nucleotide sequence and a protein sequence of Yid C from *E.Coli* respectively wherein Yid C is a protein that can mediate membrane protein assembly in bacteria (see a review from Chen *et al.*, Biol. Chem., 383, 1565-1572, October 2002).

However, the specification fails to adequately describe that a nucleic acid encoding a gene product having 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO:413 and a gene product having 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO:413. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998).

In this instant case, although the specification adequately describes SEQ ID NOs: 220 and 413, the specification fails to adequately describe that a nucleic acid encoding a gene product having 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO:413 and a gene product having 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO:413. It is also unclear whether SEQ ID Nos: 220 and 413 are a partial cDNA sequence and a partial protein sequence or not. Since a nucleic acid encoding a gene product having 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO:413 can be read as an kind of nucleic acid nucleic acid encoding a gene product having 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO:413 and a gene product having 70% amino acid identity to a gene product

comprising the amino acid sequence of SEQ ID NO:413 can be read as a polypeptide having 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO:413, a nucleic acid encoding a gene product having 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO:413 and a gene product having 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO:413 recited in claims 133 and 134 encompass numerous unknown and unidentified nucleic acids and polypeptides that miss from the disclosure. It is unclear what kind of functions of these nucleic acids and polypeptides have and whether these nucleic acids and polypeptides have the same function as YidC does. Therefore, the general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

With limited disclosure provided by the specification, the skilled artisan cannot envision all above possible nucleic acids and polypeptides and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co.* Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what e has not conceived. See *Fiddes v. Baird,* 30 USPQ2d 1481, 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated nucleic acid consisting of SEQ ID No: 220 and a gene product

consisting of SEQ ID No: 413 meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

4. Scope of Enablement

Claims 45-48, 50-56, 133, and 134 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing certain sensitized microbial cell as recited in claims 45-56, 133, and 134 by expressing a sub-lethal level of an antisense nucleic acid comprising a nucleotide sequence of SEQ ID NO: 60, does not reasonably provide enablement for producing any kind of sensitized microbial cell as recited in claims 45-48 and 50-56 by expressing a sub-lethal level of an antisense nucleic acid complementary to a nucleic acid in any kind of microbial cell, wherein said nucleic acid encodes a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of SEQ ID NO: 60, and does not reasonably provide enablement for producing any kind of sensitized microbial cell as recited in claims 13 and 14 by expressing a sub-lethal level of an antisense nucleic acid complementary to a nucleic acid in any kind of microbial cell, wherein said nucleic acid encodes a gene product having at least 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO: 413. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance to produce any kind of sensitized microbial cell as recited in claims 45-48 and 50-56 by expressing a sub-lethal level of an antisense nucleic acid complementary to a nucleic acid in any kind of microbial cell, wherein said nucleic acid encodes a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of SEQ ID NO: 60, and produce any kind of sensitized microbial cell as recited in claims 133 and 134 by expressing a sub-lethal level of an antisense nucleic acid complementary to a nucleic acid in any kind of microbial cell, wherein said nucleic acid encodes a gene product having at least 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO: 413. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether any kind of sensitized microbial cell recited in claims 45-48, 50-56, 133, and 134 can be produced by the method recited in claims 45 and 133.

Claims 45-48 and 50-56 are directly to a method for identifying a compound which reduces the activity or level of a gene product required for proliferation of a microorganism by

expressing a sub-lethal level of an antisense nucleic acid complementary to a nucleic acid in any kind of microbial cell, wherein said nucleic acid encodes a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of SEQ ID NO: 60. Claims 133 and 134 are directed to a method for identifying a compound which reduces the activity or level of a gene product required for proliferation of a microorganism by expressing a sub-lethal level of an antisense nucleic acid complementary to a nucleic acid in any kind of microbial cell, wherein said nucleic acid encodes a gene product having at least 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO: 413. The specification only describes that SEQ ID No: 60, which is a nucleotide sequence of Yid C from *E.Coli* wherein Yid C is a protein that can mediate membrane protein assembly in bacteria (see a review from Chen *et al.*, Biol. Chem., 383, 1565-1572, October 2002). Applicant's declaration under 37 C.F.R § 1.132 filed on August 11, 2003 (see page 3, fifth paragraph) showed that a sensitized *E. Coli* can be produced by expressing a sub-lethal level of an antisense nucleic acid comprising a nucleotide sequence of SEQ ID NO: 60. However, the specification does not provide a guidance to produce any kind of sensitized microbial cell as recited in claims 45-48 and 50-56 by expressing a sub-lethal level of an antisense nucleic acid complementary to a nucleic acid in any kind of microbial cell, wherein said nucleic acid encodes a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of SEQ ID NO: 60 and produce any kind of sensitized microbial cell as recited in claims 133 and 134 by expressing a sub-lethal level of an antisense nucleic acid complementary to a nucleic acid in any kind of microbial cell, wherein said nucleic acid encodes a gene product having at least 70% amino acid

identity to a gene product comprising the amino acid sequence of SEQ ID NO: 413. Although SEQ ID No: 60 can be used as an antisense nucleic acid in *E.coli,* since a microbial cell can be defined as an organism of microscopic size including bacteria, fungi, algae, and protozoa, it is unclear whether SEQ ID NO: 60 can be used as an antisense nucleic acid in any kind of microbial cell as recited in claims 45-48, 50-56, 133, and 134 because the specification does not provide an evidence to show that SEQ ID NO: 60 is highly conserved in all microbial cell and can be used as an antisense nucleic acid in any kind of microbial cell. In fact, sequence searching shows that highly conserved region of SEQ ID No: 60 only can be found in bacteria strain *Shigella flexneri* 2a, *E. Coli,* and *Salmonella enterica suvbsp. Enterica serova Typhi* (see attached sequencing search results. This suggests that SEQ ID NO: 60 can not be used as an antisense nucleic acid in any kind of microbial cell. Furthermore, there is no evidence to show that any nucleic acid complementary to a nucleic acid encoding a gene product having 70% amino acid identity to a gene product comprising the amino acid sequence of SEQ ID NO:413 as recited in claims 13 and 134 can be used as an antisense nucleic acid in any kind of microbial cell.

With these unpredictable factors, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. These undue experimentation at least includes to test whether a nucleic acid comprising a nucleotide sequence of SEQ ID NO: 60 can serve as an antisence nucleic acid in any kind of microbial cell and whether any nucleic acid complementary to a nucleic acid encoding a gene product having 70% amino acid identity to a gene product comprising the

amino acid sequence of SEQ ID NO:413 can be used as an antisense nucleic acid in any kind of microbial cell.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 45-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 45 is rejected as vague and indefinite because it is unclear that "an antisense nucleic acid complementary to a nucleic acid" and "an antisense nucleic acid comprising a nucleotide sequence of SEQ ID NO: 60" are the same molecule or not. Please clarify.

Response to Arguments

8. Applicant's arguments with respect to claims 45-56 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. No claim is allowed.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270 (before January 13, 2004) or 571-272-0746 (after January 13, 2004). The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
December 31, 2003

BJ FORMAN, PH.D.
PRIMARY EXAMINER